

\* NOTICES \*

The Japanese Patent Office is not responsible for any damages caused by the use of this translation.

1. This document has been translated by computer. So the translation may not reflect the original precisely.
2. \*\*\*\* shows the word which can not be translated.
3. In the drawings, any words are not translated.

---

(The domain of a bibliography + summary + claim)

---

- (19) [Country of Issue] Japanese Patent Office (JP)  
(12) [Official Gazette Type] Open patent official report (A)  
(11) [Publication No.] JP,8-268907,A  
(43) [Date of Publication] October 15, Heisei 8 (1996)  
(54) [Title of the Invention] Periodontium regeneration accelerator  
(51) [International Patent Classification (6th Edition)]

A61K 38/22 ACK

31/65

47/32

47/36

// (A61K 38/22 ACK

31:65 )

[FL]

A61K 37/24 ACK

31/65

47/32

47/36

[Request for Examination] Un-asking.

[The number of claims] 3

[Mode of Application] FD

[Number of Pages] 5

(21) [Filing Number] Japanese Patent Application No. 7-100682

(22) [Filing Date] March 31, Heisei 7 (1995)

(71) [Applicant]

[Identification Number] 000106324

[Name] Sunstar, Inc.

[Address] 3-1, Asahimachi, Takatsuki-shi, Osaka

(72) [Inventor(s)]

[Name] Takemura Dait

[Address] 13-17-502, Koyanagi-cho, Ibaraki-shi, Osaka

(72) [Inventor(s)]

[Name] Matsuura Masahiro

[Address] 13-72-301, Makita-cho, Takatsuki-shi, Osaka

(72) [Inventor(s)]

[Name] Fujii Yuko

[Address] 2-10-1, Kami-hamuro, Takatsuki-shi, Osaka

(57) [Abstract]

[Objects of the Invention] Offer of the periodontium regeneration accelerator used in order to reproduce the periodontium destroyed by the periodontitis etc.

[Elements of the Invention] The periodontium regeneration accelerator which blended the cell growth factor and the tetracycline antibiotic.

---

[Claim(s)]

[Claim 1] The periodontium regeneration accelerator which blended the cell growth factor and the tetracycline antibiotic with the support permitted on the physic as an active principle [a claim 2] The periodontium regeneration accelerator according to claim 1 whose cell growth factor is a platelet origin cell growth factor [a claim 3] The periodontium regeneration accelerator according to claim 1 or 2 with which the support permitted on the physic contains one or more sorts chosen out of xanthan gum, a sodium alginate, and a carboxyvinyl polymer

---

[Translation done.]

\* NOTICES \*

The Japanese Patent Office is not responsible for any damages caused by the use of this translation.

1. This document has been translated by computer. So the translation may not reflect the original precisely.
2. \*\*\*\* shows the word which can not be translated.
3. In the drawings, any words are not translated.

---

## DETAILED DESCRIPTION

---

[Detailed Description of the Invention]

[0001]

[Field of the Invention] this invention relates to the periodontium regeneration accelerator used in order to reproduce the periodontium destroyed by the periodontitis etc.

[0002]

[Description of the Prior Art] Conventionally, as a cure for a periodontitis, the technique a scaling etc. mainly removes a plaque is used, and when critical, the \*\*\*\* surgery treatment is made. Although the chemotherapy by the antibiotic is tried recently, although these treatments are policies effective in preventing advance of a periodontitis, they do not restore and reproduce the destroyed periodontium positively.

[0003] In order that the epithelial cell on the front face of a gum may cover the parodontal pocket with the conventional technique before reproducing a periodontium although the periodontium has the structure where it does not see, in other organizations of adhering by firm combination of the fiber nature the hard tissue (root of tooth) and the tissue (gum) minded the periodontium (down growth of an epithelium), the epithelial tissue and a connective tissue normal between root of teeth cannot be reproduced, and a strong combination does not arise. For this reason, the reconstitution of the parodontal pocket is carried out easily, as a result repullulation of a periodontitis and the regression of a gum arise in a high frequency.

[0004] On the other hand, the down growth of an epithelium is suppressed as technique of reproducing a normal fiber nature combination, with radical-plane processing by (1) citric acid, and the high barrier layer of (2) biocompatibilities, and application \*\* to the part of the lead anagenesis method (the GTR method) and (3) cell growth factors which secure the space for periodontium regeneration is proposed. However, since the technique of (1) receives a cell, \*\*\*\* and the technique of (2) have the trouble where the difference of the success percentage by the way person is large, in order to arrange a barrier layer by the surgical treatment among the parodontal-pocket section. Although the technique of (3) has conquered the trouble of (1) and (2), since it may give side effects other than a known action to a living body by a lot of medication, it needs to give more effective medication conditions and needs to reduce the dose.

[0005] In view of such a situation, this invention person took lessons from the periodontium regenerant which was excellent in effectiveness, a stability, and operability, and piled up the research zealously.

[0006]

[Means for Solving the Problem] this invention offers the periodontium regeneration accelerator which comes to blend the cell growth factors which promote the regenerative function of the cell which constitutes the periodontium, and a tetracycline antibiotic into the same support.

[0007] Although the cell growth factor had the effect which reproduces the organization destroyed by gum disease also by independent medication, it was prescribing a tetracycline antibiotic for the patient simultaneously, and the activity of a cell growth factor was promoted and it found out that a multiplication-effect was acquired by regeneration of the periodontium.

[0008] There are growth factors, such as a platelet origin cell growth factor, an epidermal growth factor, and a cell growth factor for insulins, among the growth factors used by this invention, and especially a platelet origin cell growth factor is desirable. These growth factors are marketed from

U.S. Gibco and U.S. Upstate Biotechnology, and can come to hand easily. These loadings have [ in a platelet origin cell growth factor and an epidermal growth factor ] 0.1 - 1 desirable % of the weight 0.01 to 0.1% of the weight at an insulin Mr. cell growth factor.

[0009] Moreover, in a tetracycline antibiotic, the minocycline and the doxycycline are desirable. These are marketed from U.S. Sigma and can come to hand easily. These loadings have 0.1 - 10 desirable % of the weight (potency).

[0010] the support by which this invention is permitted on the physic according to a conventional method -- uniting -- pharmaceutical forms, such as gel and the solution, -- it can carry out -- especially -- It excels [ in a stability ] and is desirable when the support permitted on the physic contains one or more sorts chosen out of xanthan gum, a sodium alginate, and a carboxyvinyl polymer. 0.01 - 5.0 % of the weight of loadings is desirable.

[0011] In this way, the periodontium regeneration accelerator of this invention can be used by applying to the parodontal pocket after the \*\*\*\* surgery treatment or the radical-plane \*\*\*\* treatment directly. Although it can fluctuate suitably by the symptom and site which should be treated, the desired periodontium regeneration effect is demonstrated with the dosage of 1 - 10micro g of numbers at once as an amount of peptides.

[0012]

[Example] The example of an experiment and a case of the operation are given to below, and this invention is explained to it still in detail.

[0013]

(Example 1 of prescription)

A platelet origin cell growth factor 1mg Minocycline 1 g xanthan gum 1 g Energy Make Water \*\* \*\*\*\* Amount 100 g (example 2 of prescription) platelet origin cell growth factor 1mg doxycycline 1 g alginic-acid Na 0.5g energy Make Water \*\* \*\*\*\* Amount 100 g (example 3 of prescription) An epidermal growth factor 1mg minocycline 1 g alginic-acid Na 1 g energy Make Water \*\* \*\*\*\* Amount 100 g (example 4 of prescription) epidermal growth factor 1mg doxycycline 1 g carboxymethyl-cellulose 0.5 g energy Make Water \*\* \*\*\*\* Amount 100 g (example 5 of prescription) insulin Mr. cell growth factor 10mg doxycycline 1 g polyvinyl pyrrolidone 1 g energy Make water \*\* \*\*\*\* Amount 100 g (example 6 of prescription) insulin Mr. cell growth factor 10mg minocycline 1 g xanthan gum 0.5 g energy Make Water \*\* \*\*\*\* Amount 100 g (example 7 of prescription)

A platelet origin cell growth factor 1mg Minocycline 1 g carboxyvinyl polymer 1 g Energy Make Water \*\* \*\*\*\* Amount 100 g (example 8 of prescription) platelet origin cell growth factor 1mg doxycycline 1 g carboxyvinyl polymer 0.5g energy Make Water \*\* \*\*\*\* Amount Each 100 g is \*\*\*\*ed, a purified water is added and agitated, and gel is \*\*ed.

[0014] What blended only support by the antibiotic independent (contrast 1) (contrast 2), and the thing (contrast 3) blended by the cell growth factor independent were diluted with the gel of the examples 1, 3, 5, and 7 of example of examination (1) periodontal-membrane-fibers blast-cell propagation activity examination (technique) prescription, and the prescription same as a contrast 10,000 times to the Dulbecco strange method MEM (DMEM) culture medium which contains fetal calf serum 1%, and those proliferation-of-cells activity was measured. That is, it \*\*\*\*ed on the DIN tin block created from the evulsion gear tooth of the cow which sterilized the periodontal-membrane-fibers blast cell of the Homo-sapiens origin, the after [ one week ] cell was exfoliated with the trypsin solution, and the number of cells was measured. A result is shown in Table 1.

[0015]

[Table 1]

検体	細胞数( $\times 10^4$ 個/ $1\text{cm}^2$ )	
処方例1	対照1	3.3(100.0)
	対照2	3.5(106.1)
	対照3	4.7(142.4)
	検体	5.9(178.8)
処方例3	対照1	3.2(100.0)
	対照2	3.3(103.1)
	対照3	4.1(128.1)
	検体	5.2(162.5)
処方例5	対照1	3.8(100.0)
	対照2	3.8(100.0)
	対照3	4.1(107.9)
	検体	5.0(131.6)
処方例7	対照1	3.7(100.0)
	対照2	3.8(102.7)
	対照3	4.8(129.7)
	検体	5.7(154.1)

( ) 内は、各処方の対照1群を100とした値

The diluent of each prescription showed the promotion action to propagation of a periodontal-membrane-fibers blast cell so that clearly from the result of Table 1.

[0016] (2) The pathological assay considered the action of periodontium regeneration accelerator prescription various kinds to the periodontium renewal process after the action (technique) dog flap operation to the periodontium renewal process after the dog flap operation. According to the conventional method, the flap operation was given the vertical jaw premolar section which established the healthy periodontium by brushing etc. In this case, in order to consider as the reference point of next pathology histology-quantification, before and after deleting an alveolar bone, the reference point called notch to a radical plane was given. The analyte prescribed for the patient the gel of the examples 1, 3, 5, and 7 of prescription shown in the example of prescription, and prescribed for the patient what blended only support with the right-hand side vertical jaw by the antibiotic independent by the same prescription as a contrast (contrast 1) (contrast 2), and the thing (contrast 3) blended by the cell growth factor independent. After the operation \*\*\*\*ed the gum valve and gave the protection by a suture and the pack for one week. After evaluation extracted \*\*\*\*\*ed week [ 4th ] after the operation and created the preparation by the conventional method, it measured the distance between each part grades under the microscope using the ocular micrometer, and quantified it on the following criteria. A result is shown in Table 2.

[0017]

[Equation 1]

1: 上皮のダウングロス率 (%) =

$$\frac{\text{骨削除前のノッチ下縁から上皮の再根尖側までの距離}}{\text{骨削除の長さ}} \times 100$$

2: 線維性付着率 (%) =

$$\frac{\text{線維が垂直および斜走する部分の長さ}}{\text{骨削除の長さ}} \times 100$$

[0018]

[Table 2]

検体	上皮のダウングロース率	線維性付着率
処方例1	対照1	10.6(100.0)
	対照2	33.7(100.0)
	対照3	34.7(103.0)
	検体	39.2(116.3)
処方例3	対照1	41.7(123.7)
	対照2	10.5(100.0)
	対照3	35.2(100.0)
	検体	36.3(103.1)
処方例5	対照1	38.5(109.4)
	対照2	10.3(98.1)
	対照3	38.5(109.4)
	検体	39.7(112.8)
処方例7	対照1	33.8(100.0)
	対照2	10.8(100.0)
	対照3	35.1(103.8)
	検体	38.6(114.2)
処方例7	対照1	40.7(120.4)
	対照2	10.6(100.0)
	対照3	33.7(100.0)
	検体	34.0(100.9)
処方例7	対照1	38.2(113.3)
	対照2	10.2(96.2)
	対照3	10.1(95.3)
	検体	38.2(113.3)
処方例7	対照1	41.7(123.7)
	対照2	9.8(92.5)
	対照3	10.1(95.3)
	検体	9.8(92.5)

( ) 内は、各処方の対照1群を100とした値

As shown in Table 2, various prescription showed the promotion action clearly to the rate of fiber nature adhesion while they suppressed the down growth of an epithelium.

[0019] 3) The pathology histology-determination appraisal method considered the action of a periodontium regeneration accelerator to the periodontium renewal process after the action (technique) ape flap operation to the periodontium renewal process after the ape flap operation. The flap operation was given the vertical jaw premolar section which established the healthy periodontium by brushing etc. according to the conventional method. In this case, in order to consider as the reference point of next pathology histology-quantification, before and after deleting an alveolar bone, the reference point called notch to a radical plane was given. The analyte prescribed for the patient the gel of the examples 2, 4, 6, and 8 of prescription shown in the example of prescription, and prescribed for the patient what blended only support with the right-hand side vertical jaw by the antibiotic independent by the same prescription as a contrast (contrast 1) (contrast 2), and the thing (contrast 3) blended by the cell growth factor independent. After the operation \*\*\*\*ed the gum valve and gave the protection by a suture and the pack for one week. After evaluation extracted [ postoperative 3 month ] \*\*\*\*\*-ed and created the preparation by the conventional method, it measured the distance between each part grades under the microscope using the ocular micrometer, and quantified it on the following criteria. A result is shown in Table 3.

[0020]

[Equation 2]

$$\text{新生セメント質の形成率(\%)} = \frac{\text{ノッチ下縁から新生セメント質の最歯冠側端までの距離}}{\text{セメントエナメル境からノッチ下縁までの距離}} \times 100$$

[0021]

[Table 3]

検体	新生セメント質形成率(%)	
処方例2	対照1	23.3(100.0)
	対照2	24.2(103.8)
	対照3	26.7(114.5)
	検体	29.4(124.5)
処方例4	対照1	20.9(100.0)
	対照2	21.3(101.9)
	対照3	23.1(110.5)
	検体	25.9(123.9)
処方例6	対照1	23.4(100.0)
	対照2	24.6(105.1)
	対照3	26.0(111.1)
	検体	28.1(120.1)
処方例8	対照1	23.2(100.0)
	対照2	24.1(103.8)
	対照3	25.8(112.0)
	検体	26.9(115.9)

( ) 内は、各処方の対照1群を100とした値

As shown in Table 3, various prescription promoted formation of a neogenesis cement notably.  
[0022]

[Effect of the Invention] According to this invention, the periodontium regeneration accelerator excellent in operability, a stability, and effectiveness is obtained.

---

[Translation done.]